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Reply to the Editor:

We thank Dr. Edmunds for his comments on our data and insights. We totally agree with his opinion that the systemic aprotinin remains a proven method to preserve hemostasis and that subsequent studies of topical aprotinin are needed to confirm the efficacy and reveal the mechanism of preserving hemostasis during and after cardiopulmonary bypass (CPB).

When comparing advantages of two protocols of systemic aprotinin (high-dose and low-dose), however, we are faced with two specific questions: Is the inhibition of kallikrein activity needed during CPB to preserve hemostasis? Is the fibrinolysis inhibition in the systemic blood needed after the end of CPB? The kallikrein activity, which is significantly inhibited by the high-dose protocol and not by the low-dose protocol, could accelerate the intrinsic clotting system as pointed out by Dr. Edmunds, consequently activating and damaging platelets by thrombin generation[1] during CPB. Although some reports[2] indicated that high-dose aprotinin significantly reduced clotting activity during CPB, a recent study[3] showed that the predominant clotting activity is generated through the extrinsic pathway, which is in accordance with our observation in the pericardial cavity.[4] Thus activation of the kallikrein system is probably of minor importance for thrombin generation during CPB. These conflicting results make the clinical relevance of kallikrein inhibition on preserving hemostasis questionable. The second conflicting point is the importance of fibrinolysis inhibition in the systemic blood *after* CPB on preserving hemostasis, which could be achieved only by the high-dose protocol. Our previous study[5] demonstrated that fibrinolysis stimulating activity is locally intensified inside the thoracic cavity after operation, which is quite in contrast to the rapidly disappearing activity in the systemic blood after CPB. These data suggest that hemostatic fibrin sealing on the wound surface could be attacked by fibrinolysis more from the side of the wound surface than of systemic blood after CPB. According to this speculation, the topical use of aprotinin on the surgical wound at the end of operation makes sense, and the importance of maintaining systemic high concentrations of aprotinin after CPB has been challenged.

As stated by Dr. Edmunds, nothing is ever simple in the hemostatic mechanism of patients after CPB. Every finding will give us a clue to reveal the mechanism of hemostasis and improve therapy.

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12/8/63008

The location of station 11 pulmonary lymph nodes

To the Editor:

Anatomically, station 11 pulmonary lymph nodes are described by Naruke[1] as interlobar and are present between the lobar bronchi in either lung. These nodes are originally described by Rouvière[2] as being present in the angle between the upper and middle lobe bronchi on the right. These were termed the "superior interlobar nodes." The "inferior interlobar nodes" are located below the middle lobe bronchus, lie between it and the lower lobe bronchus, and are also referred to as station 11 lymph nodes. In the left lung the lymph nodes in station 11 lie in the angle between the left upper lobe and lower lobe bronchi. Rouvière[2] termed these nodes the "left interlobar lymph nodes." Borrie[3] referred to these superior interlobar nodes as the "sump nodes" of the right lung and the interlobar nodes as the sump nodes of the left lung. It is thus difficult to accept inclusion of the lymph nodes of station 11 as being hilar nodes, which are typically described as being along either main stem bronchus. Unfortunately, Yano and his colleagues[3] have considered station 11 nodes as hilar nodes in their recent publication. Unless these aforementioned authors have a compelling, rational explanation for the inclusion of the nodes of station 11 with those of station 10 as hilar nodes, the data generated as to the difference in survival and sites of recurrence between those patients with metastatic involvement of "hilar" nodes and those patients with only "lobar" (stations 12 and 13) nodal involvement cannot be accepted without serious reservation.

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Reply to the Editor:

As Dr. Shields pointed out, the words "hilar lymph nodes" are usually applied to the nodes along the main bronchus (No. 10). However, the concept of "hilar" lymph nodes slightly differs among investigators, because the definition of "hilus of the lung" itself is vague. For example, the Japan Lung Cancer Society considered the "hilar" lymph nodes to include main bronchial (No. 10), interlobar (No. 11), and lobar (No. 12) nodes, whereas the "intrapulmonary" lymph nodes include segmental (No. 13) and subsegmental (No. 14) nodes.[1] Therefore, to describe the location of regional lymph nodes precisely, one should use numbers in the lymph node map of Naruke, Suemasu, and Ishikawa.[2, 3]

The purpose of our study was to clarify whether pathologic N1 disease is a uniformly intermediate group or a mixed group of potentially early-stage disease and advanced-stage disease. There were few reports concerning the significance of N1 level in the postoperative prognosis. We have concentrated our interests on the better survival of patients with pathologic N1 disease involving only lymph nodes within the lobar bronchus (Nos. 12 and 13), which was arbitrarily referred to as "lobar" N1 disease. In contrast to these "lobar" N1 nodes, interlobar lymph nodes (No. 11), especially lying along the intermediate stem bronchus in the right side, were referred to as "hilar" N1 nodes as well as No. 10 lymph nodes. Therefore, we did not claim that interlobar (No. 11) nodes were anatomically included in hilar nodes. We divided pathologic N1 disease into two groups, that is, "lobar" N1 disease (Nos. 12 and 13) and "hilar" disease (Nos. 10 and 11), only to analyze the significance of N1 level in survival. On the basis of on our results, however, the subclassification of N1 nodes, "lobar" and "hilar," might be rationally acceptable regarding postoperative survival.

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